CHARACTERIZATION OF MOLECULAR MODE OF DNA SYNTHESIS DURING BREAK INDUCED REPLICATION

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Abnormal repair of DNA double strand breaks can lead to Gross Chromosomal Rearrangements (GCRs) that are the root cause for abnormal genetic and cellular functions that lead to cancer. DSBs left with only one of the two broken DNA ends must be repaired by Break Induced Replication (BIR). BIR requires extensive DNA replication which is very mutagenic. BIR model proposes that the junction made between the invading broken chromosome and the donor molecule substitutes for the origin of DNA replication. This initiates the assembly of a replication fork, which copies the donor sequence till the end of the donor chromosome. The assembly of a replication fork and the mode of DNA replication during BIR remains untested. Our study using 2-Dimensional electrophoresis demonstrates that BIR follows an unusual type of DNA synthesis forming “bubble” like replication intermediates. Also our result using molecular combing experiments demonstrates that BIR follows a “conservative mode” of DNA synthesis. This unusual kind of DNA replication could explain the highly mutagenic nature of BIR.

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